REMARKS

Reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

In the final Office Action, claims 1, 2, 10-24 and 31-37 stand rejected under 35 U.S.C. § 112, first paragraph, both, in the sense of a "written description" rejection (c.f. *Vas-Cath Inc. V. Mahurka,* 19 USPQ2d 11111), as well as allegedly not having enabled the invention throughout the claimed scope.

Further, claims 1, 2, 10-24 and 31-37 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out the claimed subject-matter.

Further, claims 1, 2, 10-24 and 31-37 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bengtsson in view of Fredholt *et al.* and further in view of Harris *et al.* and Florin-Robertsson *et al.* (The former rejection of original claims 1-24 under 35 U.S.C. § 103(a) as being unpatentable over Bengtsson in view of Harris *et al.* and Fredholt *et al.* and Florin-Robertsson *et al.* had also been maintained.)

(2) Claim Amendments in view of the indefiniteness rejections raised.

In new claims 38-59 presented herewith, new independent claims 38 and 39 clarify that the claimed pharmaceutical composition is stable for at least 18 months at room temperature, which means that the pharmaceutical composition exhibits an extended shelf life.

Support for such amendment can be found in examples 3 and 4 of the Application as originally filed, where it has been shown that the titre of the composition remains substantially the same (meaning that the composition is "stable") within 4 days after

dispensing of the composition into glass or plastic containers. This test format was specifically chosen by the Applicant to investigate the risk of adsorption of the peptide onto the container walls (which is a short-term phenomenon, compared to microbial degradation). From the results reported in examples 3 and 4, it should be absolutely self-explanatory that no major titre loss could have occurred also *before* the expiry of the 4 days, as –if this was the unlikely case- such loss would have been followed necessarily by a still more unlikely, strictly corresponding titre restoration. Hence, it can be reasonably assumed that the claimed solutions are stable also for periods shorter than the four-day term reported in examples 3 and 4.

In other words, the claimed solutions are not susceptible to adsorption on container walls at RT (a fact which is reflected –as per Examiner's suggestion in the second full paragraph of page 7 of the Office Action- by the proposed claims 38 and 39 to the extent that these claims are committed to the declared absence of adsorption inhibitors), meaning that the claimed solutions display short-term stability.

On top of that, the claimed solutions also display long-term stability, an aspect which was investigated by the Applicant in example 5, where the substantially constant titres after up to 18 months demonstrate that neither adsorption onto container walls, nor degradation takes place for at least 18 months, even at RT. Note that the resistance to degradation is reflected – as per Examiner's suggestion in the second full paragraph of page 7 of the Office Action- by the proposed claims 38 and 39 to the extent that these claims are committed to the declared absence of degradation inhibitors, i.e. of antioxidants and antimicrobial additives.

Applicant submits new independent claims 38 and 39 overcome the indefiniteness rejection and, accordingly, it should be withdrawn.

In the newly submitted claims, the other indefiniteness rejections have also been addressed, in particular the "active principle" has been replaced by "peptide", the nonspecific recitation of "it" has been replaced by "the composition" and the grammatical structure of the sentence has been improved pointing out that adsorption inhibitors are inhibitors "which prevent" adsorption. Still further, the limitation as to the pH range (namely 3.5-6) called for by the Examiner in the paragraph bridging pages 5 and 6 of the Office Action has been introduced. The proper support for such amendment should not be in dispute, as it has already been identified in the Office Action itself.

As to claim 39, Applicant believes that the use of consisting of should make it clear "by definition" that <u>everything</u> else, i.e. *inter alia* also preservatives, is excluded. Hence Applicant's understanding is that the additional recitation of the particular absence of preservatives solicited by the Examiner is intended to better circumscribe the gist of the claimed invention, while leaving the scope of the claim unamended, i.e. introducing a "non-limiting limitation" into claim 39.

Applicant has refrained from the introduction of such a "non-limiting limitation" until now, since this type of "seeming" but legally ineffective limitation is often objected to by most of the world's Patent Offices for various reasons (mainly clarity). If this is not the case here with the USPTO, Applicant offers the solicited amendment, should the same be regarded still as compulsory by the Examiner.

<u>(3) "Written Description" and "Incommensurate scope" Rejections.</u>

Though severable, these two rejections are treated together here, as Applicant believes that both of them are overcome by the newly proposed limitation in claims 38 and 39, according to which the buffer imparts a pH range of 3.5-6.

Clearly, with this limitation, no longer is *any* type of known buffer claimed nor is *any* conceivable ratio of buffer salts claimed. The reduced pH range recited in claims 38 and 39 makes a selection as to the nature of suitable buffers and as to their dosage. E.g., well-known couples of buffer salts designed for alkaline or for very acidic pH ranges are implicitly, yet inevitably, excluded.

Since at the filing date of the Application, the choice and dosage of a suitable addition of buffer to arrive at a particular pH window was without any doubt a measure falling within the normal skills of one of ordinary skill in the art. There can be no conceivable doubt that Applicant, who provides two completely separate and distinct examples of how to achieve this aim, was indeed in possession of what he is now claiming. Hence, the "written description" rejection is believed to have been overcome, and its withdrawal is solicited.

As to the "enablement" rejection, Applicant believes that it is not true that: "*The specification does not even suggest that any other buffers or mg ranges are contemplated by the invention*", as is stated towards the end of the first full paragraph of page 5 of the Office Action.

Quite to the contrary. The application states at page 4, lines 5-7, that:"For maintaining such a pH value (namely 3.5-6, as said immediately before), the composition shall contain a suitable buffer such as, **for example**, citric acid / disodium phosphate dihydrate or citric acid / trisodium citrate dihydrate." That is to say, the invention does indeed also contemplate other buffers, provided that these buffers and their relative amounts actually added enable access to the envisaged pH range.

Furthermore, Applicant has provided two explicit examples, spelling out *in extenso* of how to achieve such a goal in practice, a teaching which is deemed to be reasonably

enabling to one of ordinary skill in the art. Patent protection would be almost obsolete if Applicants were pinned down, in their claims, to almost fingerprints of the very conditions identified in their working examples – a format which could be easily designed around by one and all, provided that he or she is nothing but possessed of sufficient skill to correctly choose and dose a buffer.

(4) Obviousness Rejections.

Applicants respectfully request reconsideration of the obviousness rejection maintained and re-applied in the Office Action at issue, because, in Applicant's view, Bengtsson, Harris, Fredholt and Florin-Robertsson, in the combination outlined by the Examiner, neither suggest nor render obvious the embodiments of the invention recited in each of new independent claims 38 and 39. This is particularly true as in the evaluation of obviousness, any hindsight knowledge of the invention must be definitely excluded.

As the Examiner has pointed out in the first paragraph on page 10 of the Office Action, he feels that Bengtsson teaches that preservatives may be excluded, while they would not necessarily have to be excluded. The Examiner has also challenged Applicant's prior observation that the skilled man (who would be a scientist rather than a lawyer) would not reasonably take the particular definition of the legal monopoly granted to Bengtsson as a scientifically founded disclosure, unless not supported by specific examples actively pointing to a particular teaching.

Assuming for the sake of argument the value which one of ordinary skill would attribute to the particular format and sequence of Bengtsson's claims, it must not be forgotten that the fictitious reader normally takes as a watershed criterion for the assessment of inventive step, a man of ordinary skill in the art, i.e. a woman or man with scientific background in the particular technical field at issue.

Since Bengtsson nowhere identifies nor even alludes to any short-term or long term studies, the skilled artisan would certainly not deduce from Bengtsson that peptide solutions of the type here at issue could be kept stable up to 18 months. There is virtually no way (not even with hindsight) to construe the disclosure of Bengtsson to arrive at this specific teaching.

On top of that, it should be noted that construing Bengtsson in the eyes of the skilled man, does not mean reading Bengtsson *tout court* and exploring the semantic scope of his disclosure, but does mean instead, applying the background knowledge which is typical of the man skilled in the art and which is reflected by the generally accepted text books which the skilled man can reasonably supposed to have studied, to successfully complete his scientific degree.

Since both, "Martindale's Complete Drug Reference" and "Physical Principles of Pharmacy" contain clear warnings as to the susceptibility of small and medium-sized proteins to container wall adsorption (and suggest suitable "preservatives" as remedies), and since according to Bengtsson preservatives could or could not be included, the skilled man would understand that the preservatives (i.e. adsorption inhibitors) *should* be included in all those cases where the general background knowledge deems them compulsory, e.g. if a large volume of solution was to be divided into many small doses held in glass or plastic containers. Likewise, the skilled man would assume, always based on his background knowledge, that preservatives of the degradation inhibitor type would normally be compulsory, if not in every case, than at least in those instances where stable preparations of extended shelf life were to be obtained. In other words, a fictitious person taking the presence of any preservative in Bengtsson as completely optional and not

linked, instead, to the particular circumstances envisaged, cannot be regarded as a man "skilled in the art".

This is true even more so in view of the fact that the skilled man who is supposed to read Bengtsson is necessarily aware of Harris (not only because Harris was cited in the discussed combination of documents, but more importantly because Harris was previously **published** pertinent art), such that an expert would read Bengtsson in the light of Harris – and reasonably ***not*** the other way round- such that he would understand that the optional addition of a quarternary ammonium preservative or disinfectant (claim 1 of Harris), e.g. benzalkonium chloride (column 3, line 6 of Bengtsson) would be compulsory in all those embodiments of Bengtsson for which –in view of the intended use- stability and storage problems (column 2, line 11 of Harris) were to be avoided.

In other words, even if not always possible, the preservatives of Bengtsson would nevertheless be deemed compulsory by the skilled reader in the specific case now spelled out in Applicant's claim, namely if a stability lasting 18 months was to be achieved.

The skilled man's interpretation of Bengtsson as above would of course not be overturned by any analogy-assumption made with respect to Florin Robertsson, as Florin-Robertsson himself (see column 2, lines 55-66) contains a clear and explicit *disclaimer* of any analogy assumption whatsoever in those instances where the nature of the protein is no longer the same. Accordingly, Florin-Robertson could not override the prejudice arising from Harris, as Harris (not Florin-Robertson) is specifically focussed on the peptide at issue. Neither would a reading of Fredholt change the skilled man's interpretation of Bengtsson as explained above, since it would not make sense to the skilled man, who is aware through Harris of possible problems with long term storage stability (*...up to 18*

months), to draw any conclusion whatsoever from preparations which, like the ones of Fredholt, are reported to have been prepared on the spot for comparative testing.

All in all, since the skilled man, unless taking the benefit from the hindsight knowledge acquired from the claimed invention, would normally not interpret specific passages of a document (Bengtsson) against the overall gist of the document ("preservatives are necessary in all those cases where the skilled man's background knowledge or specific teachings, i.e., Harris, so require") and neither would he construe specific passages (claim 1 of Bengtsson) unreasonably beyond the specific context in which they were made, it comes out that the invention was not obvious to one of ordinary skill in the art in the light of the references cited.

For at least the reasons outlined above, Applicant respectfully submits that each of new independent claims 38 and 39 are independently patentable over the prior art cited. The dependent claims as submitted herewith are deemed patentable by the virtue of their dependency on claims 38 and 39. Hence, Applicants respectfully request reconsideration and withdrawal of the obviousness rejections.

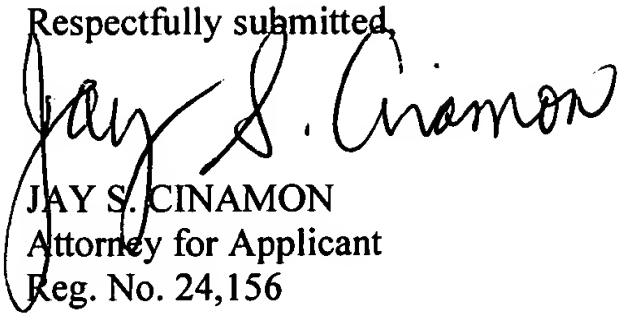
(5) Conclusion.

The Examiner is invited to contact the undersigned attorney if a further telephonic communication is believed to be helpful in advancing the examination of the present invention.

Since all of the rejections are deemed to have been overcome, and since the claims are deemed to distinguish over the art, the issuance of a Notice of Allowance is solicited.

The Office is hereby authorized to charge any additional fees or credit any overpayments to Deposit Account No. 01-0035.

Respectfully submitted,



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